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Interactive effects of specific fine particulate matter compositions and airborne pollen on frequency of clinic visits for pollinosis in Fukuoka, Japan

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A R T I C L E I N F O

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A B S T R A C T

Background: Previous studies have revealed the interactive effects of airborne pollen and particulate matter on the daily consultations for pollinosis, but it is uncertain which compositions are responsible. This study aimed to investigate the interactive effects of specific $PM_{2.5}$ compositions and airborne pollen on the daily number of clinic visits for pollinosis in Fukuoka.
Methods: We obtained daily data on pollen concentrations, $PM_{2.5}$ compositions, $PM_{2.5}$ mass, gaseous pollutants (SO_2, NO_2, CO, and O_3), and weather variables monitored in Fukuoka between February and April, 2002–2012. In total, 73,995 clinic visits for pollinosis were made at 10 clinics in Fukuoka Prefecture during the study period. A time-stratified case-crossover design was applied to examine the interactive effects. The concentrations of $PM_{2.5}$ and its compositions were stratified into low (< 15th percentile), moderate (15th–85th percentile), and high (> 85th percentile) levels, and the association between airborne pollen and daily clinic visits for pollinosis was analyzed within each level.
Results: We found a significant interaction between specific $PM_{2.5}$ compositions and airborne pollen. Specifically, the odds ratio of daily clinic visits for pollinosis per interquartile increase in pollen concentration (39.8 grains/cm^2) at the average cumulative lag of 0 and 2 days during high levels of non-sea-salt Ca^{2+} was 1.446 (95% CI: 1.323–1.581), compared to 1.075 (95% CI: 1.067–1.083) when only moderate levels were observed. This result remained significant when other air pollutants were incorporated into the model and was fairly persistent even when different percentile cut-off points were used. A similar interaction was found when we stratified the data according to non-sea-salt SO_4^{2-} levels. This finding differed from estimates made according to $PM_{2.5}$ and NO_3^- levels, which predicted that the effects of pollen were strongest in the lower levels.
Conclusions: Associations between airborne pollen and daily clinic visits for pollinosis could be enhanced by high levels of specific $PM_{2.5}$ compositions, especially non-sea-salt Ca^{2+}.

1. Introduction

A number of epidemiological studies have found the significant increase in the prevalence of allergic diseases worldwide, especially in developed countries (Burney, 1993). A previous study noted that the prevalences of allergic rhinitis and hay fever during 1991 in Switzerland were 13.5% and 11.6%, respectively (Wüthrich et al., 1995). Similarly, a study that targeted schoolchildren in Taichung, central Taiwan showed a dramatic increase in the prevalence of allergic rhinitis, from 5.1% in 1987 to 27.6% in 2002 (Liao et al., 2009). Exposure to airborne pollen is an important co-factor responsible for the increased incidence of allergic diseases, especially pollinosis (Wüthrich, 1989). Dispersion of pollen is often affected by climate change, where pollen counts and pollen exposure are likely to change

Abbreviations: $PM_{2.5}$, particulate matter with aerodynamic diameters less than 2.5 μm; NO_3^-, nitrate; nss-SO_4^{2-}, non-sea-salt sulfate; nss-Ca^{2+}, non-sea-salt calcium; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; CO, carbon monoxide; O_3, ozone; CI, confidence interval; ICD, International Classification of Diseases; ADS, Asian dust storm

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every year (Bajin et al., 2013; D'Amato et al., 2007; Okamoto et al., 2009; Shea et al., 2008). Pollen typically persists in the atmosphere for longer than 10 weeks after the pollen season and travel distances of over 100 km (Okamoto et al., 2009). A number of studies have recently anticipated that global climate trends to gradually change (Emberlin, 1994; McMichael et al., 2006) and facilitates the spreading of pollen (Beggs, 2004). Thus, the number of patients with pollinosis symptom is possible to increase in the future, which results in people becoming more sensitized to airborne allergen and developing more allergic symptoms (Bajin et al., 2013).

Pollen granules from Japanese cedar (*Cryptomeria japonica*) and Japanese cypress (*Chamaecyparis obtusa*) are considered the major airborne allergens causing serious pollinosis in Japan (Okuda, 2003). Severity of pollinosis increases during the pollen season, which typically spans from February to May each year, and decreases during the off-pollen season (Okamoto et al., 2009). A recent study revealed that the prevalence of pollinosis in Japan increased by approximately 9% over 10 years from 1998 to 2008 (Nakae and Baba, 2010; Saito, 2014), with considerable differences according to age group and degree of urbanization (Kaneko et al., 2005). Increases in the prevalence of pollinosis in Japan may be due in part to the increased exposure to Japanese cedar antigens (i.e., Cry j 1 and Cry j 2) and the cypress antigen, which are responsible for promoting pollinosis symptoms. Thus, pollinosis caused by airborne pollen should also take into account the amount of allergen present in the pollen (Kuribayashi et al., 2014). The quantities of Cry j 1, a major protein antigen in Japanese cedar pollen, in Japan vary throughout spring which ranged from 0.38 to 10.23 picograms per pollen grain (Saito et al., 2003). Its molecular weight is about 41 kDa and 44 kDa (Wang et al., 2012a). One previous study reported that approximately 70% of patients who are allergic to Japanese cedar are also sensitive to Japanese cypress (Ito et al., 1997). As pollen season for Japanese cypress starts later than that for Japanese cedar, pollinosis caused by Japanese cedar might be aggravated or prolonged by Japanese cypress (Kishikawa et al., 2009). Given the occurrence and potential severity of pollinosis in Japan, annual economic losses due to pollinosis increase are estimated to be 286 billion JPY (Yamamoto et al., 2010).

Sufficient evidence is available to demonstrate that the prevalence of allergic diseases has increased during periods when concentrations of atmospheric pollutants such as oxides of nitrogen, ozone, sulfur dioxide, and particulate matter, are high (Wüthrich, 1989). The Asian Dust Storm (ADS) containing small particulate matter is another potential contributor to increase the prevalence of pollinosis (Wang et al., 2012b; Yamada et al., 2014). This prevalence is particularly evident in industrial areas with high levels of organic pollutants, as well as along main roads with high levels of traffic-related air pollutants (Behrendt et al., 1992; Ishizaki et al., 1987; Wyler et al., 2000). The morphologic structure of pollen might be modulated by airborne particles, which can increase the release of allergenic contents from pollen grains (Behrendt et al., 1997; D'Amato et al., 2007). Gaseous pollutants, such as NO_2, SO_2, O_3, and CO, are also able to modify allergenic proteins in the pollen grain wall which may increase the potential of airborne pollen to exacerbate respiratory allergic diseases in susceptible subjects (Chakra et al., 2010; Ruffin et al., 1985; Wyler et al., 2000). This finding has been supported by an earlier epidemiological study that found that fine particulate matter ($PM_{2.5}$) enhanced the association between airborne pollen and daily medical consultations for pollinosis in Tokyo, Japan (Konishi et al., 2014). Similarly, the correlation between the number of patients with respiratory allergic diseases and air pollution increased significantly during the *Ambrosia* pollen season in Hungary, supporting the notion that the interaction between air pollution and airborne pollen influences human allergic diseases (Makra et al., 2014).

Although a previous study reported a significant interaction between particulate matter and airborne pollen that influences the number of daily clinic visits for pollinosis (Konishi et al., 2014), the compositions of particulate matter responsible for this increase remain unclear; in other words, it is unclear whether clinic visits for pollinosis are increased during times when high concentrations of specific $PM_{2.5}$ compositions are observed. To date, no study has examined the interactive effects of specific $PM_{2.5}$ compositions and airborne pollen on respiratory allergic diseases. The present study aimed to estimate whether there is any potential interaction between airborne pollen and the specific compositions of fine particulate matter ($PM_{2.5}$) on the daily number of clinic visits for pollinosis in Fukuoka, Japan.

2. Methods

The present study was conducted in Fukuoka Prefecture, which is the most populous area of Kyushu, the south-western island of Japan. In 2010, Fukuoka was home to approximately 5.1 million citizens (Ministry of Internal Affairs and Communications, 2015). As Fukuoka is influenced by trans-boundary air pollution, exposure to air pollution is expected to be high (Yoshino et al., 2016). During the spring (February through May), Asian dust containing fine PM and other components is typically carried to Fukuoka by wind from the desert areas of Northern China, Mongolia, and Kazakhstan (Yamada et al., 2014; Zhou et al., 1996). The climate in Fukuoka is moderate, with an annual average temperature of 16.3 °C and average humidity of 70%.

2.1. Clinic visit data

We obtained daily number of patients who were suffering from pollinosis at 10 private otolaryngology and ophthalmology clinics in Fukuoka Prefecture from February 1st through April 30th, 2002–2012. The private clinics located around Fukuoka Prefecture were recruited and one clinic per each ward was selected for participating in this study. Each clinic was not far away from the pollen monitoring station. Hence, the representativeness of private clinics participated in the study were considered to a certain extent although we have no data about socio-economic status for each ward. Data from clinic visits combined those from the first visit and revisits due to pollinosis, which is diagnosed by general practitioners in the clinics using the same criteria throughout the study area. Specific IgE tests were also conducted to differentiate the pollinosis symptoms due to Japanese cedar and Japanese cypress. Pollinosis cases were classified according to the International Classification of Disease, 10th revision (ICD-10), as J30.1. Ethical approval for this study was provided by the Ethics Committee of the Graduate School of Engineering, Kyoto University.

2.2. Pollen data

Daily pollen concentrations of both *Cryptomeria japonica* (Japanese cedar) and *Chamaecyparis obtusa* (Japanese cypress) were obtained from the pollen monitoring station located at the National Hospital Organization (NHO) Fukuoka Hospital. These two pollen species are considered the most important airborne allergens causing pollinosis in Japan (Okamoto et al., 2009). Study patients, who all live and commute within Fukuoka Prefecture, were assigned by daily pollen concentrations representing their daily exposure levels. Pollen density was measured by a gravitational method used widely in Japan that employs a Durham sampler. In this method, pollen grains adhere to vaseline-coated glass slides, which are fixed inside the Durham sampler (Kishikawa et al., 2009). Pollen counts are then standardized and expressed as the number of pollen grains per square centimeter (grains/cm^2) on the glass slide. A previous study found that numbers of airborne pollen measured by the Durham sampler at the monitoring station correlated very well with those determined by the volumetric method using a Burkard sampler ($r < 0.923$; P-value < 0.001), the latter of which is typically used in Western countries (Sasaki et al., 2009). The number of pollen grains on the vaseline-coated glass slide was daily determined except for Sunday. Readings for Saturday and